REMARKS

Claims 1,3-10 and 12-37 are currently pending in the present application. Claims 1, 3, 7, 21, 29 and 31 have been amended. The amendments more clearly define that the method does not use DNA-binding materials and precipitation occurs by adding an organic solvent. Antecedent basis for these amendments can be found on page 3, lines 13-15, page 4, lines 1-3, page 9, lines 9-10 and page 5, lines 20-21. No new matter has been introduced as a result of these amendments. Claims 38-51 are currently withdrawn.

Claim Objections

The Examiner objected to claim 1 because "extrachromasomal" in line 1 should be "extrachromosomal." Appropriate correction has been made consistent with the above.

The Examiner has objected to claim 21 objected to because of the following informalities: "comprising" in line 2 should be "comprises." Appropriate correction has been made consistent with the above.

Claim Rejections - 35 USC § 112

The Examiner has rejected claims 1, 3-10 and 12-37 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement. The Examiner contends that amended claim 1 (from which all other claims depend) includes impermissible new matter because it recites in step d): "wherein step (d) is performed prior to, after, or concurrently with step (c)," and there is no support found in the specification as originally filed. Claim 1 has been amended to remove any impermissible new matter. As such, this rejection has been rendered moot.

The Examiner has rejected claims 29-31 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that claims 29-31 improperly contain

trademark/trade names used to identify/describe a detergent and, accordingly, those claims are indefinite. Under MPEP 608.01(v), names used in trade are permissible in patent applications if in this country, their meanings are well-known and satisfactorily defined in the literature. The Tween and Triton product lines have well-established meanings as shown in the following literature. The FAO Nutrition Meetings Report Series, 1974, No. 53, Wilde *et al.* (J. Colloid Interface Sci. 1993, Vol. 155, no. 1, pp. 48-54), Blake *et al.* (Anal. Biochem. 1984, Jan:136(1): pp. 175-9), and Dickinson *et al.* (J. Colloid Interface Sci. 1999, Vol. 212, no. 2, pp. 466-473), all describe the Tween product lines as polyoxyethylated sorbitan fatty acid esters. Regarding the Triton product line, see Sigma-Aldrich catalog entry for Triton X-100 and Triton X-114, which list references dating back to the 70s & 80s that define the Triton X-Line as octylphenol ethoxylates, having the general formula of $C_{14}H_{22}O(C_2H_4O)_n$. Lastly, these terms have been claimed in numerous other patent applications. See, for e.g., U.S. Pat. Nos. 7,297,395, 6,949,258, 6,676,723, 4,994,378. The claims are presently amended to reflect their commonly known meanings, the trade names being removed from the claims for the sake of clarity. The Tween product lines are already described and encompassed earlier within claim 29, and therefore are removed only for redundancy purposes.

Claim Rejections - 35 USC §103

The Examiner has rejected claims 1,3-10, 12-30, and 32-37 under 35 U.S.C. 103(a) as being unpatentable over Little (U.S. 5,075,430) as evidenced by Sigma-Aldrich catalog entry for Trizma hydrochloride (2007), in view of Padhye *et al.* (5,658,548), Koller (U.S. 5,128,247) and Chomczynski (U.S. 5,945,515). The Examiner contends that with respect to independent claim 1, Applicant's method is essentially disclosed by Little or Padhye *et al.* In addition, using the teaching – suggestion - motivation rationale, the Examiner contends that it would have been obvious to use the nucleic acid releasing composition of Koller or the lysing solution of Chomczynski in place of the chaotropic solutions and subsequent method steps of Little or Padhye *et al.* in order to lower cost by removing the

need to purchase DNA-binding materials, and save time with fewer method steps. For the reasons given below, and in light of the amendments made to the claims herein, it is submitted that the present invention is not obvious and, in fact, is patentable over the references cited by the Examiner.

Applicants respectfully traverse the Examiner's rejection for failure to meet prima facie burden. To establish a prima facie case of obviousness, the Examiner must first make the factual determinations under Graham v. John Deere Co. That is, the Examiner must: (1) Determine the scope and content of the prior art; (2) Ascertain the differences between the prior art and the claims at issue; and (3) Resolve the level of ordinary skill in the pertinent art. MPEP §2141. Once a factual determination is articulated, the Examiner must then provide a rationale to support an obviousness rejection. MPEP §2141. Put another way, the Examiner must provide articulated reasoning with some rationale underpinning. MPEP §2142. Where the teaching-suggestion-motivation rationale is used, as in this case, the Examiner must articulate: (1) some teaching-suggestion-motivation in reference or general knowledge to combine; (2) reasonable expectation of success; and (3) whatever necessary additional findings to explain conclusion of obviousness. MPEP §2143. As will be shown below, the Examiner has failed to meet his burden in establishing a prima facie case of obviousness.

By way of brief review of the prior art, Little discloses a plasmid DNA purification method by immobilizing DNA onto diatomaceous earth in the presence of a chaotropic binding buffer. However, Little does not teach the use of a ribonuclease enzyme, the precipitation of the extrachromosomal nucleic acids out of a chaotropic environment using an organic solvent, nor does it disclose how to achieve the isolation of plasmid DNA without the use of a DNA-binding material.

Padhye *et al.* teach a plasmid purification protocol that uses a resin comprising guanidine chloride (a chaotropic binding buffer) and glass particles to bind plasmid DNA to the glass. Padhye *et al.* do not disclose, however, how to achieve isolation of plasmid DNA without the use of a DNA-

binding material. Also, Padhye *et al.* do not disclose precipitating the extrachromosomal nucleic acids out of a chaotropic environment using an organic solvent.

Koller teaches a method of genomic DNA purification comprising lysing cells using a chaotropic nucleic acid releasing composition followed by precipitation of the DNA. The DNA is then collected and dissolved in a polyanion-containing protein dissociating composition. RNAse may be added to facilitate removal of unwanted RNA. Koller does not teach a method for recovering substantially purified extrachromosomal nucleic acid nor does it teach the removal of substantially all of the chromosomal nucleic acids. See specification p. x, lines x-x. Instead, the method taught in Koller uses a chaotropic composition to lyse the cells, which contaminates the extrachromosomal DNA because it releases both genomic and extrachromosomal DNA into the lysate. Once the genomic and extrachromosomal DNA is released into the lysate, it is further processed to remove the RNA (if desired) and proteins. The end result is the isolation of both genomic and extrachromosomal DNA, but not substantially purified extrachromosomal DNA.

Chomczynski teaches a method for simultaneous isolation of genomic DNA, RNA and proteins comprising dissolving cells in a chaotropic lysing solution, which releases genomic DNA into the lysate, followed by precipitation of genomic DNA, RNA, and proteins. Chomczynski does not disclose a method for recovering substantially purified extrachromosomal nucleic acid nor does it teach the removal of substantially all of the chromosomal nucleic acids.

According to the Examiner, the claimed method of isolating extrachromosomal nucleic acids is essentially disclosed by Little or Padhye *et al.* with the exception of using an RNAse (Little), which is disclosed in Padhye *et al.* and Koller as a way to remove unwanted RNA. However, both Little and Padhye *et al.* have other unaddressed deficiencies. They both teach away from the use of an entirely liquid-based system. Instead, they teach the use of a DNA purification method that uses DNA-binding

materials. In addition, they both fail to disclose the step of precipitating the extrachromosomal nucleic acids out of a chaotropic environment by adding an effective amount of organic solvent.

Furthermore, the Examiner contends that an ordinary skilled artisan seeking an efficient method to purify plasmid DNA would have been motivated to use the nucleic acid releasing composition of Koller or the lysing solution of Chomczynski (and the related DNA precipitation steps) in place of the chaotropic solutions and subsequent method steps of Little or Padhye *et al.* According to the Examiner, this is because the reagents and methods of both Koller and Chomczynski remove the need to purchase and/or prepare the Celite or glass particles of Little and Padhye *et al.*, respectively. Therefore, the Examiner contends, it would have been obvious for the skilled artisan to do this because of the known benefit of isolating extrachromosomal DNA at a lower cost and/or with fewer method steps to save time (and the potential loss of the desired DNA).

To begin, in combining the methods of Little, Padhye *et al.*, Koller and Chomczynski, it is unclear what process steps of the Little and Padhye *et al* process are to be used, and which ones are not. The same goes for Koller and Chomczynski - it is not clear which steps are to be used as replacements, and which ones are not. Indeed, chaotropic solutions are used in more than one step of the Little and Padhye *et al* methods, so one would not know from which point in the process would the subsequent method steps be replaced. At any rate, the nucleic acid releasing composition of Koller and the lysing solution of Chomczynski are both chaotropic solutions used to lyse the cells. If those compositions were used to lyse the cells in Little or Padhye *et al.*, the result would be contamination of the extrachromosomal DNA with genomic DNA. Substantially impure extrachromosomal DNA would be obtained, and the step of removing substantially all of the chromosomal nucleic acids would not occur regardless of whether the subsequent processing steps followed the teachings of Little, Padhye *et al.*, Koller, or Chomczynski.

Additionally, the Examiner has not provided a reason as to why the nucleic acid releasing composition of Koller or the lysing solution of Chomczynski should not be used as they are taught to be used. Why can we simply replace the chaotropic binding buffers and subsequent method steps of Little or Padhye *et al.*? While Applicant agrees that a benefit arises when less materials are used or the method encompasses fewer process steps, this is a common benefit that every inventor of a method seeks to achieve. This "motivation" does not provide the technical knowhow to develop Applicant's invention. Indeed, the Examiner has not shown that the ordinary artisan at the time of filing possesses the knowledge and skills rendering him capable of combining the prior art references. Further, the Examiner has not shown or articulated why one would have a reasonable expectation of success in combining the prior art; i.e., why the combination of the references would result in a successful process. Accordingly, the Examiner does not satisfy the standard of a "clear articulation of the reason(s) why the claimed invention would have been obvious," and has not established a prima facie case of obviousness.

Examiner also relies on Little and Padhye *et al.*, references that Examiner claims to essentially disclose Applicants' invention, which are 10+ years old. The art has developed various DNA purification techniques since Little (as shown by the references cited by the Examiner) and still has not come up with Applicants' method. Indeed, in viewing the state of the art spanning from Little (1991) to Padhye *et al.* (1997), the art found no way to eliminate the use of DNA-binding materials when isolating substantially pure extrachromosomal nucleic acids. Examiner has not cited to any more recent art related to isolation of substantially pure extrachromosomal nucleic acids that would suggest the knowledge of the art has progressed to the point of eliminating DNA-binding materials. Also, Examiner cited to Koller (1992) and Chomczynski (1999), both of which are methods for isolating nucleic acids (which includes both extrachromosomal and genomic DNA) and fail to isolate substantially pure extrachromosomal DNA. While viewing the art over a seven year span between

Koller and Chomczynski, the pace of technological progress was steady, but slow, and failed to suggest that the knowledge of the art had progressed to the point of isolating substantially pure extrachromosomal DNA using a liquid process similar to Koller or Chomczynski (without the use DNA-binding material). The combination of these references is not obvious to result in Applicants' invention, especially when the art has not suggested or shown the technical knowhow to do so.

CONCLUSION

In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are in form for allowance. Accordingly, reconsideration of those claims, as amended herein, is earnestly solicited. Applicants encourage the Examiner to contact their representative, Stephen R. Albainy-Jenei at (513) 651-6839 or salbainyjenei@fbtlaw.com. The Commissioner for Patents is hereby authorized to charge any deficiency or credit any overpayment of fees to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

THOMAS D. REED, *et al.*

By_____

Stephen R. Albainy-Jenei
Registration No. 41,487
Attorney for Applicant(s)
FROST BROWN TODD LLC
2200 PNC Center; 201 East Fifth Street
Cincinnati, Ohio 45202
Tel: (513) 651-6839
salbainyjenei@fbtlaw.com